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## Reply

We thank Dr. Grundtvig and colleagues for their interest in our paper (1). They have concerns regarding: 1) the mortality figures; 2) achieved drug prescription; and 3) use of diuretics in the BATTLESCARRED (NT-proBNP-Assisted Treatment To Lessen Serial Cardiac Readmissions and Death) trial (1) of hormone-guided treatment of heart failure.

1. They assert incorrect mortality figures, having misread Table 4 (1), which documents composite end points not deaths. One-year mortality was 18.9% (23 deaths) in the usual care group and 9.1% (11 deaths) in both intensively followed groups, not 16, 6, and 7 deaths, as asserted by Dr. Grundtvig and colleagues. Similarly, 3-year mortality in those under 75 years of age was 15.5% (9 deaths) in the hormone-guided subgroup and 30.9% (17 deaths) and 31.3% (20 deaths) in the other 2 groups, not 6, 6, and 12 deaths as Grundtvig and colleagues write. The correct figures are stated in the Results section and are illustrated with tabled numbers in Figure 2 (1).
2. That the prescription of angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, beta-blockade, and spironolactone was somewhat higher in the Norwegian Heart Failure Registry than in BATTLESCARRED is of interest and may reflect the younger age of registry subjects (71 years) compared with trial patients (median age: 75 to 76 years). As stated in the Methods section (1), the trial design mandated prescription of drugs to trial-based levels or intolerance in both intensively followed groups, and this principle was followed scrupulously. Intolerable side effects (commonly hypotension or azotemia) were more frequent in those over 75 years of age. Nevertheless, the proportions of patients receiving evidence-based drugs, and doses achieved, were similar to those seen in previous trials and reflect "real-life" limitations on dose escalation in this fragile group of patients. In addition, our patients all had to have clearly elevated N-terminal pro–B-type natriuretic peptide levels as an inclusion criterion, which is likely to have selected a more fragile population (more prone to drug intolerance) than those in the Norwegian registry.
3. We do not claim that our results mandate escalation of diuretic doses in the presence of persistently elevated N-terminal pro–B-type natriuretic peptide levels. In fact, final diuretic doses were similar in both intensively managed groups (Table 3 of our study [1]), although they were more frequently adjusted (both up and down) in the hormone-guided group. However, it is clear that patients under 75 years of age were frequently able to tolerate increased doses of diuretics without hypotension or azotemia, and in the case of the hormone-guided group, this occurred together with improved 3-year survival. We make no claim that higher diuretic dose directly improved mortality. The fact that diuretic dose is associated with increased mortality in the Norwegian registry is no surprise given that decompensation is the prime trigger for increasing doses. However, such an association in no way indicates that diuretics cannot be appropriately and beneficially increased in addition to neurohormonal blockade provided proper clinical surveillance (to avoid hypotension, azotemia, and other problems) is sustained.

Finally, we agree that any shift in clinical management requires good evidence and suggest that this is now accumulating with 4 randomized controlled trials consistently suggesting that at least younger (age <75 years) patients with heart failure may benefit from consideration of serial B-type peptide levels in monitoring and adjusting treatment.

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# Practical Considerations for 1-Day Stress-Only Myocardial Perfusion Protocol

Chang et al. (1) explore the advantages of technetium (Tc-99m) sestamibi and Tc-99m tetrafosmin 1-day stress-only perfusion imaging. This is an invaluable protocol in cardiac nuclear stress testing, especially in light of the growing concern surrounding radiation exposure secondary to physician-ordered imaging tests (2). Additionally, as the investigators mention, it decreases overall cost, decreases radiopharmaceutical doses, and takes less time for the patient in comparison to a study that also requires rest imaging (1).

Chang et al. (1) argue that the 1-day stress/rest Tc-99m protocol is preferable, because of the option to forego rest images when stress perfusion scans are normal. It is notable, however, that when this protocol requires rest images, there is a longer wait time between images secondary to higher tracer uptake during the low stress image when compared with the wait time between images in a 1-day rest/stress Tc-99m protocol (3).

Their report (1) states that stress imaging should be followed by rest imaging "only in patients with equivocal or clearly abnormal

studies." We believe that in abnormal studies, the proposed protocol may underestimate defect reversibility, particularly if there is inadequate delay between injections. Stress-induced hypoperfusion may not have fully resolved at the time of rest imaging. Additionally, absolute myocardial perfusion is higher with stress, so the proportion of Tc-99m taken up by the myocardium is higher following the smaller stress dose than the higher rest dose; this would tend to undermine the swamping effect.

Even with normal myocardial perfusion on stress images, it is important to evaluate all clinical data, planar images, gated images, and attenuation correction images, including computed tomography scans, to determine if the patient needs rest imaging. We agree that in addition to normal myocardial perfusion, patients must have normal cavity size to rule out reversible dilation, and an ejection fraction >50% with normal wall motion (1) to rule out post-ischemic stunning. We also propose that patients with normal stress images should also have rest images if the patient has angina during the stress test, hypotension with exercise, or ST-segment depressions meeting ischemic criteria during stress (4). Ischemic electrocardiograph changes, particularly during adenosine infusion, have been shown to be associated with an increased risk of future cardiac events (5), even with normal myocardial perfusion.

Still, there are other markers of significant coronary artery disease that, if noted, require rest images even with homogenous left ventricular perfusion on stress images. More specifically, patients with increased lung-to-heart uptake ratio (6) or increased right ventricular uptake (7) on stress images should have rest images before a study is considered nonischemic. Patients with calcification in the left main artery on computed tomography attenuation images should also have rest images even with normal stress images.

We believe that this protocol is suitable for patients with low-likelihood disease and no history of myocardial infarction. Rest images should be obtained if any of the aforementioned observations are made in the stress images. These precautionary measures may help avoid providing false reassurance to patients and providers when performing stress-only perfusion imaging.

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# Normal Stress-Only Versus Standard Stress/Rest Myocardial Perfusion Imaging

## Similar Patient Mortality With Reduced Radiation Exposure

We read the paper by Chang et al. (1) and accompanying editorial (2) with great interest. The insightful single-center study addresses safety of normal stress-only myocardial perfusion imaging (MPI). However, it raises some concerns.

Careful examination of the paper suggests a conundrum. Annualized crude death rate for the stress-only MPI group is significantly lower than stress and rest MPI. However, after adjustment for clinical factors associated with mortality (Table 3 of Chang et al. [1]) this difference in crude mortality, which is lower in the stress-only group, disappears. This, despite the fact that the stress-only group was significantly less likely to have these risk factors associated with higher mortality, both in aggregate (Table 1 of Chang et al. [1]) (mean number of risk factors: $1.33 \pm 1.1$ vs. $1.57 \pm 1.1$, $p < 0.001$) and for each individual risk factor. The fact that the stress-only group was older by 1.1 years cannot possibly, it seems, explain this effect of adjustment.

The study, although large, is retrospective and has all of the limitations of retrospective studies (3,4).

The stress-only study was performed in patients weighing <200 lbs. Hence, the study's findings may be applicable to this subset of patients only, and furthermore, with the growing epidemic of obesity, its applicability will be further reduced. Chang et al. (1) did not indicate what percentage of these patients needed to undergo additional rest MPI. Additionally, height and/or body mass index were not considered in deciding stress-only protocol. With the same 200 lbs weight, a patient whose height is 60 inches would have a body mass index of 39.1 kg/m$^2$, whereas for a patient whose height is 72 inches, it would be 27.1 kg/m$^2$. The former patient (short and stubby) may present a significant challenge for stress-only MPI.

The end point was all-cause mortality derived from Social Security Death Index. Chang et al. (1) did not mention how many patients did not have a social security number and hence were lost to follow-up.

We do not have incidence of unstable angina pectoris, nonfatal myocardial infarctions, hospitalizations, revascularizations, and